UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,468	10/18/2004	Søren Weis Dahl	16778.10a.1.	2832

22913 7590 05/15/2007

WORKMAN NYDEGGER
(F/K/A WORKMAN NYDEGGER & SEELEY)
60 EAST SOUTH TEMPLE
1000 EAGLE GATE TOWER
SALT LAKE CITY, UT 84111

EXAMINER
KIM, ALEXANDER D

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
05/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,468	DAHL ET AL.	
	Examiner	Art Unit	
	Alexander D. Kim	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *9-31,40-41,44,46-56 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 32-39, 42-43, 45, 57, 59 and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/18/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (mailed on 01/11/2007), Applicants filed a response received on 03/12/2007. Claims 1-75 are pending in this instant Office action.

Election

2. Applicant's election without traverse of Group I, Claims 1-60, is acknowledged. Claims 61-75 are withdrawn from consideration as non-elected inventions. Claims 9-13 (Claims 14-31 and 40-41 dependent therefrom), 44, 46-56 and 58 are withdrawn. Thus, Claims 1-8, 32-39, 42-43, 45, 57 and 59-60 will be examined herein.

Applicant elected the species: (a) Green Fluorescent Protein for a complementation protein, (b) FKBP12 and FRB for partners A and B, and (c) a protein normally associated with nuclear material or nuclear components as the anchor protein, without traverse. It is noted that the species election recited in (c) is not needed because the claims disclosing the species of an anchor protein are withdrawn, that is Claims 51-56.

Priority

3. The instant application is a 371 filing of the International Application No. PCT/DK03/00266 filed on 04/22/2003. The Examiner notes that the requirements of national stage entry of the instant application had been completed (note assigned U.S.

filing date) within 30 months of the earliest claimed priority date; the related international application includes both a search report and a preliminary examination report.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to a foreign patent applications: PA 2002 00591 filed on 04/19/2002 (Denmark) with English translation, PA 2002 00896 filed on 06/13/2002 (Denmark) with English translation, PA 2002 01029 filed on 07/01/2002 (Denmark) with English translation, and PCT DK02/00882 filed on 12/19/2002 (Denmark) with English translation.

Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in Denmark (PA 2002 00591) filed on 04/19/2002. A claim for priority under 35 U.S.C. 119(a)-(d) cannot be based on said application, since the PCT/DK03/00266 application was filed more than twelve months thereafter.

Information Disclosure Statement

4. The information disclosure statement (IDS) filed on 10/18/2004 has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Compliance with Sequence Rules

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to fully comply with the

requirements of 37 C.F.R. 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

The Figure 16 contains many amino acid sequences. Labeling using a SEQ ID NO must be inserted into the brief description of the drawings or into the Figure directly.

The polypeptide sequences in the specification require appropriate SEQ ID NOs in p. 48 bottom; p. 61, line 27; p. 62, line 27; and p. 63, line 20.

If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID No.

Objections to the Specification

6. The specification is objected to because of the following informalities:

The specification is objected to because the title is not descriptive of the claims. A new title is required that is clearly indicative of the invention to which the claims are

drawn (see M.P.E.P. § 606.01). The examiner suggests the following new title, for example:

---A cell useful for drug screening by translocation dependent complementation---

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-8, 32-39, 42-43, 45, 57 and 59-60 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 1 recites "the N-terminal" and "the C-terminal". There is insufficient antecedent basis for this limitation in the claim. It is unclear if the claims are limited to the one specific species disclosed in the specification or to any other N-terminal or C-terminal fragment of a complementation protein. Clarification is required.

b) Claim 5 recites "the first terminal fragment" and "the second terminal fragment". There is insufficient antecedent basis for this limitation in the claim. It is unclear if the claims are limited to the one specific first or second terminal fragment disclosed in the specification or to any other terminal fragment of a complementation protein. Clarification is required.

c) Claims 1 and 5 recite "close apposition", which is a relative term, which renders the claim indefinite. The term "close" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear how close is considered as a close apposition between two proteins. Clarification is required.

d) Claims 1 and 5 recite "the full functional protein" There is insufficient antecedent basis for this limitation in the claim. It is unclear if the claims are limited to the one specific function of a said protein or to include any other function of the protein. The term "full functional protein", or alternatively fully functional protein, is also relative term. The determination of fully functional and not fully functional depends on which function is being used as point of reference. Clarification is required.

e) Claims 32, 35 and 38 recite the term "fused in frame". It would be clear if the nucleic acid is fused in frame. However, it is unclear what is encompassed by the term in frame when two proteins are fused together. Clarification is required.

f) Regarding claim 57, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-8, 32-39, 42-43, 45, 57 and 59-60 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a cell comprising a first conjugate comprising a first protein (or a first protein and interaction partner A) and a N-terminal fragment of complementation protein; and a second conjugate comprising a second protein (or interaction partner B) and the C-terminal fragment of the complementation, wherein said first and second conjugate is located in different cellular location, wherein the first and the second protein bind to each other, and said complementation protein fragments forms fully functional protein when they are brought into close apposition.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical

name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical Inc. v. Gen-Probe Inc.* (CAFC (2002) 63 USPQ2d 1609).

The instant specification teach a cell expressing a first conjugate with N-terminal fragment of EGFP, EYFP or E[F64L]YFP and a second conjugate with C-terminal fragment of EGFP, EYFP or E[F64L]YFP using expression vectors of Table 4, p. 86 for monitoring a translocation and interaction of two proteins inside the CHO cell. However, the breadth of claims include any cell comprising: a first conjugate comprising any protein (as a first protein) fused to any fragment of any complementary protein; and a first conjugate comprising any protein (as a second protein) fused to any fragment of any complementary protein, wherein said first and second is located in any parts of the cellular location including any organelles (i.e. inside and/or membrane of the organelle within eukaryotic cell), wherein two complementary protein are brought together and forms functional protein. The prior art by Ghosh et al. (2000, J. Am. Chem. Soc., vol.

122, p. 5658-5659) and Remy et al. (1999, Proc. Natl. Acad. Sci. USA, vol 96, pages 5394-5399) teach cells encompassed by the very broad claims. The specification discloses a cell comprising a first conjugate with a certain specific N-terminal fragment of EGFP, EYFP or E[F64L]YFP and a second conjugate with a specific C-terminal fragment of EGFP, EYFP or E[F64L]YFP using expression vectors of Table 4, p. 86. The prior art and the instant specification do not describe any host cell comprising: a first conjugate comprising any protein (as a first protein) fused to any fragment of any complementary protein; and a first conjugate comprising any protein (as a second protein) fused to any fragment of any complementary protein sufficiently. Furthermore, regarding a complementary protein, any N-terminal and any C-terminal fragment of EGFP, EYFP or E[F64L]YFP without size limitation, for example, two consecutive amino acids as a N-terminal fragment and a whole sequence minus the said N-terminal two amino acids as a C-terminal would form a full functional protein when they are brought together. However, it won't be useful for measuring a protein interaction because there is not difference in C-terminal fluorescent property by the addition of said N-terminal. Also, there is no way of knowing if these fusion protein(s) will be stably express when any encoding genes are fused together and retain a native binding property between the first protein and the second protein. A cell of instant specification and prior arts do not describe a genus cell, and also do not sufficiently represent the correlation between the structure and function of claimed genus that is any host cell comprising: a first conjugate comprising any protein (as a first protein) fused to any fragment of any complementary protein; and a first conjugate comprising any protein (as a second

protein) fused to any fragment of any complementary protein, wherein said first and second is located in any parts of the cellular location including any organelles (i.e. inside and/or membrane of the organelle within eukaryotic cell), wherein two complementary protein are brought together and forms functional protein. Thus, the instant specification and the prior art cannot describe the structure of a very broad claimed genus and one skilled in the art would not be in possession of the claimed genus by the instant specification.

9. Claims 1-8, 32-39, 42-43, 45, 57 and 59-60 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for a CHO cell expressing a first conjugate with N-terminal fragment of EGFP, EYFP or E [F64L] YFP and a second conjugate with C-terminal fragment of EGFP, EYFP or E [F64L] YFP using expression vectors of Table 4, p. 86 for monitoring a translocation and interaction of two proteins inside the CHO cell, wherein first and second conjugates comprising β-catenin:TCF4 interaction, or FRBP12:FRB interaction which is inducible by rapamycin (ARIAD Pharmaceuticals), does not reasonably provide enablement for a cell comprising: a first conjugate comprising any protein (as a first protein) fused to any fragment of any complementary protein; and a first conjugate comprising any protein (as a second protein) fused to any fragment of any complementary protein, wherein said first and second is located in any parts of the cellular location including any organelles (i.e. inside and/or membrane of the organelle within eukaryotic cell), wherein two complementary protein are brought together and forms functional protein.

The specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use of the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The nature of the invention is drawn to a cell expressing a first conjugate with N-terminal fragment of EGFP, EYFP or E[F64L]YFP and a second conjugate with C-terminal fragment of EGFP, EYFP or E[F64L]YFP using expression vectors of Table 4,

p. 86 for monitoring a translocation and interaction of two proteins inside the CHO cell. However, the breadth of claims are drawn to a genus cell comprising: a first conjugate comprising any protein (as a first protein) fused to any fragment of any complementary protein; and a first conjugate comprising any protein (as a second protein) fused to any fragment of any complementary protein, wherein said first and second is located in any parts of the cellular location including any organelles (i.e. inside and/or membrane of the organelle within eukaryotic cell), wherein two complementary protein are brought together and forms functional protein. The "reassembly processes are contingent upon the proper choice of a dissection site within a protein" (see Ghosh et al. 2000, bottom left column, page 5658); thus, any fragment of two complementary proteins forming a fully functional protein when they are brought together, which is encompassed by the instant claims are unpredictable. Applicants teach a CHO cell expressing a first conjugate with N-terminal fragment of EGFP, EYFP or E[F64L]YFP and a second conjugate with C-terminal fragment of EGFP, EYFP or E[F64L]YFP using expression vectors of Table 4, p. 86 for monitoring a translocation and interaction of two proteins inside the CHO cell, wherein first and second conjugates comprising β-catenin:TCF4 interaction, or FRBP12:FRB interaction which is inducible by rapamycin (ARIAD Pharmaceuticals). The prior art by Ghosh et al. (2000, J. Am. Chem. Soc., vol. 122, p. 5658-5659) and Remy et al. (1999, Proc. Natl. Acad. Sci. USA, vol 96, pages 5394-5399) teach only a E. coli and CHO cells having a first and a second conjugates as encompassed by the claims. However, applicants and prior arts disclose no direction or guidance on how to make and use a claimed genus cell as described above having any

first and second protein having affinity to each other and any fragment of any complementary protein. Thus, the specification and prior art fail to describe how to make and use the claimed genus sufficiently. Thus, it is unpredictable for any cell encompassed by the claims for one skilled in the art to make and use the full scope of claims. For all of the above reason, it would require undue experimentation necessary for a claimed genus cell.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claim 1-8, 32-39, 42-43, 45, 57 and 59-60 are rejected under 35 U.S.C. §101 because the claimed invention is directed to non-statutory subject matter. Claim 1 and 5, as written, does not sufficiently distinguish over any cell(s) as they naturally exist because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206, USPQ 193 (1980). The claims encompass any cell with a protein comprising a multi subunit (or domain) with different polypeptides and/or nucleic acids. For example, a ribosome is a multimer having many subunits, wherein the subunit contains many polypeptides and many nucleic acids. Each subunit exists in different location in a cell, binds to each other to

form a fully functional ribosome; thus, meets the limitations of claims. The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated" or "purified" as taught by the specification. See M.P.E.P. § 2105.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-8, 32-39, 42-43, 57 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by reference by Ghosh et al. (2000, J. Am. Chem. Soc., vol. 122, p. 5658-5659).

The instant claims are drawn to a cell comprising a first conjugate comprising a first protein (or a first protein and interaction partner A) and a N-terminal fragment of complementation protein; and a second conjugate comprising a second protein (or interaction partner B) and the C-terminal fragment of the complementation, wherein said first and second conjugate is located in different cellular location, wherein the first and the second protein bind to each other, and said complementation protein fragments form a fully functional protein when they are brought into close apposition.

Ghosh et al. teach a E. coli BL21 (see bottom left column, p. 5659) comprising a N- and C-terminal fragments of GFP with each fragment containing leucine zipper as shown in Figure 1, p. 5658, that is designated as NZGFP and CZGFP. NZGFP and CZGFP of Ghosh et al. has 6-residue and 4-risidue linkers. (see bottom of right column, p. 5658 to top left column, p. 5659). The leucine-rich hydrophobic and acidic and basic interaction by the residues of leucine zipper directs the antiparallel heterodimer formation which brings two NZGFP and CZGFP together (see bottom right column, p. 5658) and the combination of two fragment results in fluorescence whereas the individual fragments are not fluorescent as shown in Figure 3, p. 5659. The location of two fragment cannot be in the same place within the cell. Thus, the E. coli of Ghosh et al. meets the limitations of Claims 1, 5-6, 32, 35 and 38-39, 42-43, 60.

The leucine zipper protein in the N-terminal fragment, the "first protein" in claim, were retained within the cell instead of excreted into the medium or the NZGFP being in cellular compartment is determined by the nature of the leucine zipper; thus, meets the limitation of Claims 2 and 3 (by the same reasons above using CZGFP).

The hydrophobicity of leucine zipper would be attracted to the hydrophobic nature of the membrane in a bacterial cell wall as well as the membrane of the nucleus in case of eukaryotic cell; thus, leucine zipper of Ghosh et al. is encompassed by an anchor protein. Also, the hydrophobic interaction force is encompassed by an interaction stimulus; thus, meeting the limitations of Claims 4, 7-8, 57.

The cell of Ghosh et al. teach the NZ was appended to the C-terminal of NGFP (as a first or as second protein) and CG was appended to the N-terminal resides of

CGFP (as a second or as a first protein) (see bottom of right column, p. 5658 to top left column, p. 5659); thus, meeting the limitations of Claims 33-34 and 36-37.

Thus, the E. coli of Ghosh et al. meets the limitations of Claims 1-8, 32-39, 42-43, 57 and 60.

12. Claims 1-8, 32, 42-43, 45, 57 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by reference by Remy et al. (1999, Proc. Natl. Acad. Sci. USA, vol 96, pages 5394-5399).

Remy et al. teach a CHO cell transfected with FRB-F[1,2] fusion protein and FKBP-F[3] which binding of these two fusion protein is stimulated by the rapamycin, wherein the F [1-3] is a dihydrofolate reductase (DHFR) as shown in Figure 1, page 5396. The complementation of F[1,2] by F[3], which is located in different part of the CHO, form fully functional DHFS when they are associated by the stimulus of rapamycin. Thus, the CHO cell of Remy et al. meets the limitations of Claims 1, 5-6, 32 42-43, 45, 57 and 59.

The first protein (FRB-F or FKBP-F fusion protein) or the second protein (FRB-F or FKBP-F fusion protein) expressed in the cell of Remy et al, is retained within the cell instead of excreted into the medium, for example; thus, first or the second protein cellular compartmentalization is determined by the nature of the first or the second protein that is meeting the limitation of Claims 2 and 3.

The hydrophobic side chain of an amino acid(s) in the fusion proteins of Remy et al. would be attracted to the hydrophobic nature of the membrane in a bacterial cell wall

as well as the membrane of the nucleus in case of eukaryotic cell; thus, the fusion proteins of Remy et al. are encompassed by an anchor protein in claims; thus, meeting the limitations of Claims 4, 7-8.

Thus, the CHO cells of Remy et al. meets the limitations of Claims 1-8, 32, 42-43, 45, 57 and 59.

Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander D. Kim whose telephone number is (571) 272-5266. The examiner can normally be reached on 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alexander Kim
May 3, 2007

RICHARD HUTSON, PH.D.
PRIMARY EXAMINER

Notice to Comply	Application No. 10/511,468	Applicant(s) Soren et al.	
	Examiner Alexander Kim	Art Unit 1656	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: see next page.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

7. cont.

The Figure 16 contains many amino acid sequences. Labeling using a SEQ ID NO must be inserted into the brief description of the drawings or into the Figure directly.

The polypeptide sequences in the specification require appropriate SEQ ID NOs in p. 48 bottom; p. 61, line 27; p. 62, line 27; and p. 63, line 20.